average patient. It's not as onerous as nonelectrolytic type of solution that obviously plays havoc with the internal electrolyte balance. Your average anesthesiologist is going to run in two liters during most surgeries. So you know, I think that obviously especially in settings maybe put a three-liter limit on the amount of fluid used. There are devices that, basically pump systems, that do monitor fluids for you. So I mean, you can set alarms and stuff like that to achieve that if you're doing it in a hospital setting.

The other thing is that these procedures probably should be done with small hysteroscopes that basically are in the range of five millimeter scopes. Having done a bunch of studies with how you put fluid through scopes and how much fluid you can put through a scope, it's damn near impossible even in 30 minutes to put, you know, much more than two or three liters through a five millimeter scope. I mean, you just cannot do it. There's a constriction problem as far as getting fluid through even under pressure. So just the amount of fluid you can use is an issue, and you shouldn't be dilating the cervix. You're not cutting into the uterine cavity. So you should have a fairly minimal chance of getting hypervolemia. I think it should be put in as a labeling thing, as a warning and maybe suggest that cut-out point of three liters for

maximum fluid use, but I don't see it as an onerous problem as it would be with significant operative hysteroscopy.

DR. BLANCO: Do you want to say anything?

DR. SEIFER: Yes. I don't know if anyone wants to comment on the two cases that are in here with five and seven liters of fluid and how much time it took.

DR. BLANCO: Well, I was actually going to ask the company. I didn't see it, maybe I just didn't read it. Do you have any concept of how much fluid was actually infused not in those two particular cases but in most of the routine cases? It's okay to say no. Okay. Do you have it offhand that you know?

DR. CARIGNAN: Charles Carignan, Conceptus.

Typically, most procedures were done with between 500 and 1,000 ccs, many more on the lower end of that scale, and actually in our training, we emphasize a cut-off of 1500 ccs.

DR. BLANCO: Is that in your labeling?

PARTICIPANT: No.

DR. BLANCO: I was just asking if you're aware of not.

MS. DOMECUS: Give me a few minutes to look through all the pages of the labeling to see if it's in there or if it's just in the training program.

DR. BLANCO: Okay. Well, I just wondered

whether it was already in there. I mean, it appears that the panel's going to make some suggestion of some limit. I just wondered whether you had it in there or not.

MS. DOMECUS: It's already our plan.

DR. BLANCO: All right. You addressed the two biggest issues. Actually, the hypervolemia issue and the fluid. What about these other things they talk about, vaso-vagal responses, discomfort, bleeding and spotting? Those are pretty minor symptomatology. So other than labeling and appropriate counseling of the patient, I don't think it's that big of a deal, but what about the tubal perforation issue? Is there something that concerns the panel? Is there any way that that can be minimized? Anything anybody wants to talk about that?

Dr. O'Sullivan?

DR. O'SULLIVAN: Yes, a couple of things I think about that. Number 1, I think that by putting the little black knob on, they tried to at least limit the amount of times that that would happen. That's Number 1.

Number 2, many of these perforations were recognized at the time they occurred just by the feel that they had when they did them. The third thing is they were relatively asymptomatic. There didn't seem to be any bleeding associated with them, and I think if you compare that -- I mean, part of our question says in conjunction

with safety and acceptability of female sterilization procedures in general is the way I was reading that. If you compare it to some of the complications of the general, I don't think that it's any worse than anything general and maybe somewhat better.

DR. BLANCO: Okay. Go ahead.

DR. SHIRK: I want to introduce a couple things that aren't on the list that I consider possible safety issues. Okay? One would be treatment of future uterine disease. Obviously they made the comment that you can't use electrosurgical devices in the uterine cavity after these things are placed. Certainly a percentage of these women in the future are going to develop interuterine pathology that can be treated by intrascopic means, both submucosal fibroids and large endometrial polyps.

My question would be does this mean that we no longer can treat these modalities with minimally invasive surgery and have to go to hysterectomy to treat them? So that's one of my concerns.

The other concern was basically with endometrial ablation. We have a thing called post-ablation syndrome, where after tubal ligation and then you do an ablation, it occludes the tube and you get sort of a small hydrosalpinx.

My question would be by occluding both ends of

the tubes, if you have a preexisting tubal disease with distal occlusion, are you going to create a symptomatic hydrosalpinx with this thing by occluding both ends of the tubes where there's no egress point for the serus fluids? So are we going to create some problems with this procedure as far as creating problems with pelvic pain and hydrosalpinx by placing these devices?

These are obviously out of the scope of the present study, but certainly if we're looking at possible issues down the line, those two issues at least pop into my mind as possible issues.

DR. BLANCO: Okay.

DR. SHARTS-HOPKO: A concern that I have, also not on the list, is related to the question I raised earlier today about sensitivity to metals. I am a person with an extreme sensitivity to metals other than 14k gold, which is a great problem.

(Laughter.)

DR. BLANCO: You sure it's not 18?

DR. SHARTS-HOPKO: Eighteen is better.

So I don't know what happens to people with metal sensitivity when you implant metals in them.

DR. BLANCO: The other issue, you know, and I wondered about that. I was going to ask because the other issue is pelvic inflammatory disease or salpingitis. I

also would wonder if your rate of perforation in those cases might be higher just because the tube's been scarred already. I don't know exactly, other than in ithnikinidosa, how much scarring you get in this area, but it might cause for harder placement and might cause for higher rate of perforation if you have prior history of salpingitis and that may be something, another reason to consider whether those are good patients to do this on.

Anybody from this side? Dr. Noller?

DR. NOLLER: Well, having seen lots and lots of complications of laparoscopy in supposedly simple cases, based on the data that we're presented and the theoretical complications and even with my assumption that these are all going to be done under general, I still think this is probably considerably safer than laparoscopic tubal sterilization.

DR. BLANCO: Any other comments on this particular question?

(No response.)

DR. BLANCO: Let us move on to the next question.

Labeling and Training. Number 7. "For the pivotal study, the training program for investigators included: didactic materials, practice on a hysteroscopic simulator, device placement in perihysterectomy patients,

interpretation of device placement by hysteroscopy, HSG, and pelvic x-ray, and proctoring of initial device placements in sterilization patients by experienced personnel.

"The sponsor is proposing to delete the requirement for placement in perihysterectomy patients and to train investigators using hysteroscopic model. The proposed physician training program also includes proctoring of an unspecified number of initial procedures by a Conceptus-designated preceptor. Is this training program adequate?"

Anybody want to make any comments on this one? We've sort of addressed some of these issues but go ahead.

MS. LUCKNER: I think there should be some recognition of prior skills because I've heard the panelists and having known in university settings the level of skill of a variety of people, some of the problems we had in the earlier fetal monitoring studies and when that came into general practice was the level of people skilled when they were inserting the scalp electrodes and handling some of the instruments.

So I'm wondering rather than changing the five, I'd rather see better counsel from the company as far as what the candidate prerequisites as you have in some academic requirements, you have prerequisites. I think

there are some prerequisites for this skill, and if they don't come with those, then those have to be accomplished first before you go into this as almost a Level 2 ultrasound versus a Level 1.

DR. BLANCO: What would you think of -- because I was thinking of saying something in the labeling for the use. It should be used by physicians who already have training in hysteroscopic procedures, I guess.

DR. SEIFER: Operative hysteroscopy.

DR. BLANCO: I'm sorry.

DR. SEIFER: Operative hysteroscopy as opposed to diagnostic hysteroscopy. I know Dr. Shirk wants to say something about it.

DR. SHIRK: Well, I was just saying I think it's appropriate to do this. A better parallel to what went on was what went on when we did laparoscopic colectomy and you had surgeons that had no laparoscopic skills and created a horrendous amount of complications with that. So they jumped into this. I mean, I'd hate to see gynecologists being forced into doing, you know, this for competition reasons and then basically trying to do it with minimal hysteroscopic skills. I think it's safer obviously if we follow our usual learning curves and basically learn how to use the piece of equipment that we're using and then progress to an operating procedure.

DR. BLANCO: Well, it sounds like everybody agrees that you have to have some hysteroscopic skills, but you brought up about the difference between diagnostic and surgical hysteroscopic skills, and I'm not sure if every hospital staff differentiates that or not and whether you want one or the other.

DR. SEIFER: Well, just for the sake of argument, operative hysteroscopy would imply that someone has operative privileges, goes in the OR, does hysteroscopy. Others, diagnostic as opposed -- some people have it in their office. Most don't. So I don't know if that would be strong enough.

DR. BLANCO: All right. Dr. Noller?

DR. NOLLER: I have another point to make, if you want to finish this.

DR. BLANCO: Yes, then let's keep talking with this. Anybody else wants to address that issue?

DR. BROWN: The point is that, I mean, you can't have hospital credentialing be a criteria because one of the potential advantages of this is that even though many people may do it under general anesthesia, there are many people who do hysteroscopy in the office which is not going to be monitored by any hospital credentialing process.

So I would think you'd have to say something

like basic diagnostic hysteroscopic, and from what we're hearing this is analogous not to an operative hysteroscopy where you're resecting fibroids, but to diagnostic hysteroscopy. That's the diameter of it.

DR. SEIFER: It also begs the question Dr. Shirk brought up about if you find concomitant pathology, you know, what do you do? Not that we've answered that question, but it also implies a certain level of proficiency at hysteroscopy.

DR. BLANCO: Subir, what do you think?

DR. ROY: The other factor I would be interested in is this hysteroscopic model.

DR. BLANCO: Well, before we go on to that, let's finish with them. What criteria? Obviously everybody agrees that some hysteroscopic experience should be a prerequisite to utilizing this procedure, and I guess the question is -- I don't know. Dr. O'Sullivan, were you going to address that issue? I know you were going to say something. I mean, where should we go with it? Do we say diagnostic or operative or just make it general? I mean, do we want to give any guidance?

DR. O'SULLIVAN: Well, the only one you can control is operative. You can't control diagnostic. I mean, operative is easily controllable. Diagnostic is not controllable at all. I don't know what goes on out in the

communities, but if there are people out there who do diagnostic laparoscopies or think that's what they're doing and probably I suspect if they're doing that, they're doing a little bit more, and it may be dangerous in their hands. So the only thing you have control over is operative.

DR. BLANCO: Anyone else?

DR. O'SULLIVAN: And this is an operative procedure in a sense. You are guiding something that you ordinarily would never do.

DR. SEIFER: You're inserting an intervention here.

DR. O'SULLIVAN: Yes.

DR. BLANCO: All right. Anything else on that? If not, let's do Dr. Noller first because he was first.

DR. NOLLER: This is the opportunity to get these done under local anesthesia. I think that sounds wonderful. I don't think they'll be done that way unless as part of the training, if you have to do five procedures or 10 or 100, whatever the number is, let's just say five, you have to do five procedures, you say five procedures under local anesthesia and/or IV sedation, period. So if you do five under general anesthesia, they don't count. You have to do five more under local and that would be one way to try to "force" more of these into the local anesthesia which would certainly be better for women.

DR. BLANCO: Any comments on that? Gerry?

DR. SHIRK: I would agree that that's probably appropriate. I disagree that these'll be done under general anesthesia simply because competition in the marketplace by people who can do it in their offices are going to obviously push the rest of the OB/GYN population into doing it in their office, to creating an office situation to do this in or at least do it in a surgicenter basis under a local anesthetic, but I would agree that, you know, suggesting that the preceptorship under local or IV sedation is not inappropriate.

DR. BLANCO: Go ahead.

MS. LUCKNER: The other thing to keep in mind is there is a shortage with anesthesiologists and many in community hospitals are having trouble covering their surgical procedures and closing ORs because of not having enough anesthesia. So if we consider this procedure is good for women and we want to make it available to them, and local anesthesia is better for the patient, the woman, then we really should push very hard for that piece and not push a procedure that might have general anesthesia requirements.

DR. BLANCO: Well, you know, I always like to be the devil's advocate, but I guess my question with this is we're kind of sort of pushing the company to making

public policy as to how physicians utilize this particular device which somewhat limits maybe who's going to use it and may actually limit the women who are able to use it. It may be that somebody starts doing it under general and eventually learns enough skills to be able to do it under local. So I'm not real crazy about putting that requirement. I mean, maybe we can recommend or encourage that this procedure be tried under local, but I'd hate to make it a requirement per se.

DR. SEIFER: But one of the reasons why this has come up for expedited review is because it doesn't require general anesthesia and perhaps local or IV sedation, but I would bolster the argument that we should be trying to encourage a non-general anesthetic.

DR. BLANCO: I have no problem encouraging. I have a problem with requiring.

Dr. Noller?

DR. NOLLER: The only reason I really brought this up at all is because the information in the draft patient pamphlets and the insert and some of the comments that the company has provided suggest of course this will be done under local and I think that we disagree on how many will be done that way but certainly some will be under general, and I think we ought to push any way we can to get these done under local. I see the training issue as being

an easy way to do it. The person can do five under local with the preceptor and then never do another one. There'd be no control then, but I think if they learned to do them under local and, gee, this works, I guess you can do it under local, I've never done it before, it works, I think they're more likely to do them.

DR. BLANCO: Well, it seems like I'm severely outvoted.

DR. NOLLER: I don't know. There are an awful lot of quiet people.

DR. BLANCO: Anything else on the local anesthesia? If not, there are several other points in this question that we probably ought to address. Anything else on the anesthesia?

(No response.)

DR. BLANCO: What about the training, the number, the issue of perihysterectomy patients versus the hysteroscopic model and this level of training, number of initial procedures? Anybody want to tackle any of those?

DR. O'SULLIVAN: I think you can take out perihysteroscopy.

DR. BLANCO: You can take it out?

DR. O'SULLIVAN: Take it out.

PARTICIPANT: Yes.

DR. ROY: But if you're going to take it out,

that's where I was going with the hysteroscopic model. There are some that are just completely non-realistic being hard plastic where everything just slips right in so easily that you think it's a piece of cake. I mean, you have to have a realistic model and it can be done. There are lots of skinlike materials available.

DR. BLANCO: Well, let me interrupt you for a second. At the pleasure of the committee, we could see the hysteroscopic model. It has not been presented to FDA before this point. So that's why it hasn't been brought up. But the nice thing of being on this committee is that once we're here, if we all want to do something, we usually can get away with it, or at least I try to look at it that way. They may not.

If the committee would like to see the model, what we can do is we are getting close to break time. We can ask the company to bring their model forth and do that and look at the model in the beginning when we regroup after the short break. So it's at the pleasure of the committee.

DR. O'SULLIVAN: I vote for that.

DR. BLANCO: Do I hear support for that? Hear, hear. Anybody strongly opposed to it? Okay. Then why don't we plan during the break if you guys would bring in the model and we will take a look at it shortly after we

reconvene from the break.

All right. Leaving the question of the hysteroscopic model out, now that we've taken care of that, what about all the other issues? Any of the other issues that anybody wanted to address? I think we've sort of addressed the hysteroscopy and level of knowledge. We've talked about the hysterosalpingogram and pelvic x-ray and ultrasound added to that before. We talked about the proctoring and we sort of came on five, but is there -- go ahead.

DR. NOLLER: I think if we really want a lot of people to begin doing this, to require more than five for proctoring is almost impossible. Five is going to be hard enough for people to hit. Also, if you aren't good after five, you may never be.

DR. BLANCO: All right. Anything else that we want? I think that pretty much does that question.

DR. BROWN: I just have a question. Is it standard in terms of this kind of thing that you're potentially saying that the company forever after is going to be responsible for doing this training for every person of the 35,000 OB/GYNS, and I have some questions about the implications of that for graduate medical education, et cetera.

I mean, is there some time frame on this?

Because obviously if this turned out to be as great as it's supposed to be and became such a common procedure, you know, 15 years from now, is Conceptus still going to be teaching OB/GYN residents? I mean, I hate to bring that up, but is there some way --

DR. BLANCO: Well, I'm sure they're going to be eager to sell their devices to these people.

DR. BROWN: Right, right.

DR. BLANCO: So I think they'll probably be interested in training them. You still have to train the folks somehow.

DR. O'SULLIVAN: But they'll eventually get trained through residency training programs.

DR. BROWN: Right.

DR. O'SULLIVAN: I think it will come through that, and this is another way that it can be done because if these devices are something that the company can buy, there are devices that could be bought by residency training programs not just for this either. I think that's important, and as we get more and more into credentialing for procedures that have to be learned after training, you know, we're going to have to become a little bit innovative in how we do this kind of credentialing.

DR. BROWN: So I guess my question specifically is once Conceptus, say, has credentialed me, will I then be

allowed to teach my residents how to do this so that when they graduate from OB/GYN residency, they don't have to be credentialed by Conceptus? I'm just wondering mechanically is that how this works.

DR. BLANCO: It's up to us.

DR. BROWN: I know.

DR. BLANCO: I mean, not to have it happen but to make the recommendation that we'd like to see.

DR. BROWN: I would make the recommendation for that, that you allow, you know, somebody who knows how to do it to then teach it themselves as opposed to having to be a company-specified person to teach 35,000 people.

DR. BLANCO: But I think at the beginning, you want the company to do that and then in educational systems, you may want to open it up a little bit more.

Anybody have any major objection to that?

(No response.)

DR. BLANCO: All right. Good. We're a little early, but rather than go to the next question, why don't we just -- I'm sorry?

MS. LUCKNER: If we notice the label, we did not really discuss labeling.

DR. BLANCO: Well, we've done a lot of discussion on labeling. Bring it up.

MS. LUCKNER: No, I'm just saying as I look at

the question, we did a very nice job on the second part, training.

DR. BLANCO: Okay.

MS. LUCKNER: So I'm not sure, and I'm not sure when we will be discussing that explicitly under the heading of labeling.

DR. BLANCO: Let's do it right now. What kinds of labeling are you concerned about that you'd like to look at?

MS. LUCKNER: I think we got two. One is that is going to be consumer-driven and one that is available for physicians so that they in the guidance and counseling to what patients are good candidates for this procedure and which ones are not.

The other thing that I don't see anything about is the post-long-term follow-up requirements for this procedure. Not being a clinician or a gynecologist, I don't know whether that's a standard kind of a thing, but I know we do long-term follow-up on birth control pills and we do certain things about that and that often is in the warnings and instruction pamphlet that we received. So should there not be something about long-term management of this device? This is a device.

DR. BLANCO: Let's get it clear, because I was going to say, well, the next question has to do with that

but it really doesn't, not what you just said, not management. It has to do with following for longer years to find what the success rate of the device is over a long period of time. So what you're saying is labeling for management of these patients after they've had the device in place. Okay.

MS. LUCKNER: Exactly.

DR. BLANCO: Okay. Things like Gerry brought up about the inability to use electrocautery inside the uterus.

MS. LUCKNER: Right. Given the mobile population that we have, the burden goes on the patient to be aware that she has this device in her and what she needs to communicate with her next provider. I mean, HMOs come and go like alphabet soup. So when the patient's going to have to change their provider based on what their insurance coverage is, I want more emphasis that the patient understands her responsibility in communicating this to the next set of people who take care of her.

DR. BLANCO: Now, we know that there's an MRI compatibility and that's not a problem. That data was looked at. Electrocautery is a problem. I think this was what you brought up about metal allergy or metal sensitivity. What are some of the other things that we would like to see the patient cautioned about and make sure

that they're aware of it for their future health care? What are some other things that we can think of?

DR. ROY: Well, Dr. Noller pointed out that one in eight won't be able to have the device placed. They should at least be aware that it might take a little more effort to try to reduce that number or else not use it at all.

DR. BLANCO: Okay. Anything else that we can come up with?

DR. NOLLER: In the IUD package inserts, there's a couple of pages about, you know, if you miss your period and stuff, make sure you get a pregnancy test because you might have an ectopic. Should that be inserted in here? Personally, I'm not sure whether it should or not, but it isn't and that would be something we could think about.

DR. BLANCO: Well, I think until we have more years of data, you know, at least theoretically, you could argue that without the years of data, you don't know if this will have a lower rate of ectopic pregnancy when it does fail and eventually there will be the zero will turn to one at some point if enough of these -- well, maybe not, maybe not, maybe never will be, but potentially could be. So yes, I think that that would be another issue that the patient needs to be cautioned about and concerned about.

DR. O'SULLIVAN: I think the patients are being given like a little wallet-sized card typically of what a cardiac pacemaker is getting, and on that card should also be listed these factors and people with pacemakers are usually pretty good about bringing up their little card and actually patients given the right information, if you gave patients cards with all of their clinical information on it and they could carry these around, they would be the first ones to present them to the physician who probably will say no, I don't need that.

(Laughter.)

DR. O'SULLIVAN: I have one other question.

DR. BLANCO: All right. Well, let's make it general then. We included some but let's not exclude other possibilities. They can get together and figure out where there are some other things that the patient needs to know about for their next 40 years or 60 years of their life or whatever. So we'll leave it broad.

All right. Go ahead, Dr. O'Sullivan.

DR. O'SULLIVAN: Now, my one question, don't everybody laugh, what happens when you go through the airport? Did you guys think about that? Will this turn those machines off? How is she going to get away with that one? She's going to need the card.

MS. DOMECUS: We've had no reports of airport

security issues.

(Laughter.)

DR. O'SULLIVAN: The problem is, you may not know.

DR. BLANCO: That was Ms. Domecus. Okay. All right. Have we addressed that issue then?

DR. O'SULLIVAN: Yes. Thank you.

DR. BLANCO: Thank you.

All right. Why don't we go ahead? It's 3:25. Let's take a break, a 15-minute break. So we will reconvene at 3:40. We will look at the hysteroscopic model and do the last question, and then we'll do the voting.

(Recess.)

DR. BLANCO: Let's go ahead and get started.

We're going to go ahead and begin the last part with a little bit of presentation about the hysteroscopic model that will be used for training with this device and then finish the question and then do the next question.

Ms. Domecus?

MS. DOMECUS: We have two of the simulator kits right here to show the external and internal anatomies and we have different versions of the internal anatomy. They're in separate pouches. We have two of these. We'll start them at both ends of the table and pass them around so you can touch these things, and then at the same time,

we'll be having two people from our Professional Education Department walk you through visually the placement in the simulator.

Let me introduce those people to you now. First is Sandy Mayer, who's the director of professional education at Conceptus, and Don Gurskis, who's one of the managers in the Professional Education Department. Don will actually operate the simulator for you and Sandy will walk you through the procedure.

DR. BLANCO: Thank you.

MS. MAYER: Thank you for the opportunity to show this simulation to you. As the models are going around, you will see that they are made up of both internal and external components and if you take the pink plastic out of the wrapper, you're able to open it and see that you can put in different uterine linings to give the physician the opportunity to practice on different types of anatomy that they will encounter in their patients, from simple tubes to lateral tubes to tortuous tubes to blocked tubes, and the physician will have the experience of doing that during the total training period.

So while you're doing that, I'm going to direct your attention to Don at the monitor and the public can look at the hysteroscopic view on the screen but the panel, you can actually see what is going on if you look at the

screen. So Don is going to start the demonstration using the exact instrumentation that a physician would use in the procedure, in the like procedure with patients.

The procedure begins with the introduction of the hysteroscope with fluid so that you have distention of the uterus which is the same as you would have with the distention during the procedure. The first thing that Don does is that he looks for the visible ostium, identifies both the ostium. When he determines which ostium is the most difficult, he will determine that that is the one that he will do first and put that ostium in the center of his field of vision for visualization throughout the whole procedure.

At that time, he will put the split introducer into the working channel of the hysteroscope, maintaining distention, and when it is in, he will pull the stylus out and insert the catheter into the split introducer in the working channel of the hysteroscope. You will see that he continues to feed it down the working channel of the hysteroscope and when it is halfway in, he pulls out the split introducer, continues to feed the catheter down the working channel, maintaining visualization, until the device is in the uterine cavity, at which time, he guides it into the fallopian tube, inserting it slowly until the black positioning bump is at the entrance to the ostium.

At that point, the physician will stabilize the handle of the device against the handle of the hysteroscope, and once he has determined that the black bump is at the ostium, he will then retract the delivery catheter one click every second until it is retracted exposing the device.

Once he hits a hard stop, you see in the picture the release catheter and the notch which give you two points of visualization for device location. When the physician is pleased with the placement, he then presses a button that releases the release catheter and the device deployment when he pulls back on the device catheter with the thumb wheel, and you see device deployment. The outer coils then expand. The physician waits 10 seconds, counts to 10, to allow full expansion of the outer coil. Once the outer coil is fully expanded, you begin rotating the handle counterclockwise 10 full turns to disengage the delivery catheter from the device. Once the disengagement has happened, you gently pull the delivery catheter out of the uterine cavity.

At this point, the physician will use the hysteroscope to go in and view the number of coils trailing into the uterus with ideal placement three to eight coils, and in this case, we have one, two, three, four, five, six, seven coils. We have seven coils exposed in the uterine lining. At this point in the training, the doctor then

would turn and do the second tube and throughout the training course, they would be able to use the various anatomies that you see here, so they get practice in all types of anatomies that they will find with live patients, and again Don is doing this with the exact instruments that the doctor will use in the procedure to get them physically comfortable with everything that is going on in the procedure, and we feel that this simulation is the surrogate for the procedure in the perihysterectomy population.

I'll be glad to answer any questions. This concludes this part of the demonstration.

DR. BLANCO: Thank you very much.

Any questions? Yes? Go ahead.

DR. SEIFER: Could you just review for us what zero -- is that a 0-, 12- or 30-degree scope?

MR. GURSKIS: This is a 25-degree scope.

DR. SEIFER: Is that what you're recommending that we place it in with?

MR. GURSKIS: This can be done up with a variety of different angle scopes. The minimum requirement is that it's a five-frame scope so for the working channel, the scopes of the device can pass through. There's no requirement on an angle of the hysteroscope.

DR. SEIFER: This model is extremely clean in

the sense that it's smooth and flat, and is there any recommendation for preparing the uteri with any kind of pharmacologic medication or is that unnecessary because of when they're going to be inserted?

DR. BLANCO: Please identify yourself.

DR. COOPER: Dr. Jay Cooper.

The recommendation is that the procedure be done whenever possible during the early proliferative phase of the cycle when the endometrium is likely to be thin and not having a situation where you would have a lot of intrauterine debris.

I have personal experience performing the procedure at any time in a woman's cycle, but there's no doubt that the hysteroscopist routinely find that the early proliferative phase of the cycle is the ideal time to do this procedure.

DR. BLANCO: Go ahead.

DR. BROWN: And so for each tube, you have this whole device for each?

DR. COOPER: Yes.

DR. BROWN: Okay. So one procedure would take two of these holes?

DR. COOPER: It's a single-use disposable.

DR. SHIRK: Hey, Jay?

DR. COOPER: Yes?

DR. SHIRK: Is there different lengths of these? Because like obviously some of the flexible hysteroscopes are a lot longer than the rigid hysteroscopes.

DR. COOPER: At the present time, there's only one length and that length will accommodate to virtually any rigid hysteroscope on the market. At the present time, the recommendation is that a rigid hysteroscope is to be used, and to be perfectly frank with you, that's I think because the great majority of hysteroscopy is done with rigid hysteroscopy. The time may come that we'll find that a flexible hysteroscope might in fact be a better tool for placement, but at the present time, rigid hysteroscopy is the standard, so to speak.

DR. SHIRK: Yes. Well, I mean, with a flexible, you obviously get a zero degree situation and it's coming straight off of your end.

DR. COOPER: You're preaching to the choir. You know that.

DR. BLANCO: This is a little more subtlety probably than what our recommendation's going to be.

Any other questions? Anything on the procedure or the model?

(No response.)

DR. BLANCO: All right. Thank you very much.

I appreciate that the company did that and many thanks to the individual who put it in who I'm sure was perspiring.

(Laughter.)

DR. BLANCO: All right. Let's go ahead and move on.

Were there any other questions? Any other comments on labeling and training, Question Number 7? Go ahead, Gerry.

DR. SHIRK: I had one, I guess. We've talked about the question of in vitro fertilization after this. Do we want to put anything in the labeling about pregnancy after this and the fact that we don't know anything about this, and how should we approach these patients as far as in vitro fertilization? I mean, I think it's a big question because I don't think we have any way of answering it, but I don't know. You obviously don't want to do a study to answer the question. It's just a question I've got. How do we approach this thing? Because, you know, I really don't know if we should put some special labeling in there that if you get pregnant with this device in, that you may have severe complications of pregnancy.

DR. BLANCO: Well, but we don't really know that.

DR. SHIRK: We don't know that.

DR. BLANCO: I think that --

DR. SHIRK: We don't know that it doesn't.

DR. BLANCO: I said may. You know, a lot of what we're doing really has been for answering the question that has a lot to do with labeling, and I think the nice thing about being on the committee is that we can put forth to the FDA and the company the idea that they somehow need to address this issue, especially when we talk about the younger folks that may be in their late twenties that, you know, may have this procedure, or mid-twenties, that there needs to be some issue addressed to the fact about regret and about any other pregnancy in the future and that little information is known about what's going to happen.

I mean, we don't know. You know, the reality is what's left in there is pretty small. We've had a fair number of pregnancies with IUDs, and oftentimes they don't create that much problems once the string's out and away from the cervix, which is not a problem here.

So I think we can just make the recommendation that that issue needs to be addressed in labeling. Is that all right with everybody? Let them work it out.

DR. SHIRK: I guess the question is, an IUD obviously is an accident. I mean, you don't get pregnant with an IUD in place on purpose. Okay? But this would be on purpose with an IUD in place.

DR. SHARTS-HOPKO: You mean the in vitro part?

DR. SHIRK: Yes, IVF. I mean, the only way you're going to get pregnant is if this thing remains zero as far as number of failures is basically a deliberate rod around the obstruction. So to me, it's different between -- I mean, basically a pregnancy with an IUD in it is an accepted risk of having the IUD in, when you're deliberately doing this to go around the obstruction.

DR. BLANCO: No, but that just also brings up the issue that ideally, with appropriate counseling, we know it's going to happen. You know, it shouldn't happen.

All right. Anything else? Nancy, did you want to say something?

DR. SHARTS-HOPKO: Well, no. That was my point, that you don't want anything in the labeling that gets women to think that this is not a permanent contraceptive strategy.

DR. SHIRK: I understand, but I mean, I think that makes it permanent.

DR. SHARTS-HOPKO: Yes.

DR. SHIRK: I mean, that means that even if you decide to change your mind down the line, that we don't recommend that you do IVF, and that also comes across the people doing IVF. If you do IVF and you get a complication of pregnancy, then you're at risk legally for that complication.

DR. BLANCO: Now, somehow I think the company's probably going to have a big interest in how they word that one. So I think we can probably leave it at just that something needs to be addressed about that. How's that?

All right. Let's move on to the next question. Post-Approval Studies. Number 8. "An important finding from the longitudinal CREST Study was that the risk of sterilization failure persists for years after the procedure and varies by method of tubal occlusion and patient age.

"At present, only one- and two-year contraceptive efficacy data are available for the Essure System. Conceptus does plan to follow all Phase II and pivotal study subjects out to five years post-device placement.

"Is five years an adequate time frame for postmarketing follow-up for this device? Does the panel have recommendations about how to minimize loss to follow-up? Are other elements of a post-approval study needed?"

Who would like to tackle that one, first of all? Not overwhelming.

DR. SHARTS-HOPKO: I'll comment.

I think five years is a reasonable expectation for the company. There was something that caught my eye, and I forget which of these five volumes it was in, but you

all anticipated getting maybe a private investigator to track down your drop-outs, and I thought that was a little zealous.

(Laughter.)

DR. BLANCO: All right. Dr. Brown?

DR. LARNTZ: I don't.

(Laughter.)

DR. BROWN: I would actually take the opposite tack and say that based on the data that we now have about the CREST Study, that if they're going to be doing the follow-up for five years, I would like to see it done for longer so that you'd be able to more definitively say you don't see this acceleration that seems to start with all the other methods at five years and go up, so maybe extend it to seven years.

DR. BLANCO: On that remark, I'd like to ask Dr. Costello to come up and do two things. One is we've mentioned this acceleration issue several times, and I'd like to comment on that because I think what she's going to tell us is that there is no acceleration issue, Number 1, and then Number 2, why don't you, while you're up there, please address the issue of were there any strategies that were used in the CREST Study that helped in the maintaining follow-up of these patients that you could suggest that might be things that the company could do?

Thank you, Dr. Costello.

MS. COSTELLO: Okay. You're welcome.

First, I'd like to have you look again at Slide 6 and what you see is cumulative probabilities of pregnancy following sterilization. At year 1, that cumulative probability is a certain height but at year 2 that impedes the probability at year 1, year 2. So it's throughout the years. So it's not that it's accelerating. It's that that probability is going to increase with each year because it includes the years beforehand.

So the use of the term "accelerating" is actually really making me quite uncomfortable because that's not really what we found. Actually, when we look to the ectopic pregnancy analysis, the annual rate of pregnancies in the fourth through 10th years was actually at the same as the annual rate of pregnancies in the first three years. So their actual annual rate of pregnancies is not actually accelerating.

DR. BLANCO: So what you're saying, for somebody simple like me, what you're saying is that the rate is 1 percent year 1, it's 1 percent year 2, 1 percent year 3, 1 percent year 4, 1 percent year 5, but now you're at 5 percent?

MS. COSTELLO: Exactly.

DR. BLANCO: Because you've got each year

cumulative, right?

MS. COSTELLO: Exactly.

DR. BLANCO: So it's not accelerating, it's additive?

MS. COSTELLO: Exactly.

DR. BLANCO: Thank you.

DR. SEIFER: And just to clarify that, on Slide 6, when the slope increases, all that means is --

MS. COSTELLO: That means that by year 10, then the probability of having a pregnancy by year 10 includes the probability of having pregnancy at 1 through years 9 up until year 10.

DR. BLANCO: Were there any method for which you saw an increasing percentage of pregnancies subsequent years beyond the first 1, 2, 3, 4, or 5 years? Do you understand my question?

MS. COSTELLO: Well, if you look at the graph, it looks like possibly bipolar is the only one that seems to be increasing at a greater rate, but I would say that if you looked at that with the confidence intervals, it wouldn't appear so.

DR. LARNTZ: If I might just make a comment. The way I look at this to see if it's accelerating is I put a pencil or something at zero zero and then see if it deviates from a straight line, if it's going up from that.

Most of them don't. Actually, most of them actually curve off a bit, so they're actually, if anything, decelerating. But it's an approximate way to do that. Just take your pencil at zero zero and see, and I think with the noise, I'm sure there isn't an acceleration.

DR. BLANCO: Thank you.

MS. COSTELLO: Yes, exactly. With the noise, it may seem like bipolar is the one that might be the one that has the rate that continues the same rate each year, whereas the others may possibly seem to flatten off.

Your question about follow-up. The CREST Study filled out for each patient, they filled out a patient locator form at sterilization and then at annual follow-up, the CDC investigators sent a list of patients to the study site who were due for their annual telephone follow-up interview. So then, the nurses who have been trained at each study site attempted to call each patient about their annual interview and they've tried three times at different times of the day, and if they didn't respond, then they were still tried for the next follow-up interview.

DR. BLANCO: Okay. Any questions? Yes, Dr. Noller?

DR. NOLLER: I have another comment.

MS. COSTELLO: Anything specific?

(No response.)

DR. BLANCO: All right. Thank you very much.

DR. NOLLER: As far as the follow-up, there are a number of books and articles that have been written about increasing follow-up, and I think probably the best thing is just to talk to people that have done it. The CREST Study. We have a study that started in 1974 and we still have about 84 percent of the women, several thousand women, in it. You know, there are ways you do this, and it's well written up. In the United States right now, it's hard to lose anybody if you really, really try and you don't have to use detectives.

DR. BLANCO: Any comments? Dr. Brown, I'd like to ask you since you brought it up, but it sounds, if the rate had pretty much stayed the same in most of these other methodologies, it sounds like five years may be sufficient to really figure out whether it's changes or it's the same.

DR. LARNTZ: Well, certainly, if there's any kind of increase, we'll probably see it in five years.

DR. BLANCO: All right. So, the question is is five years adequate? Sounds like everybody thinks it is, and then Dr. Noller mentioned there are ways of minimizing loss to follow-up that would be recommended. So the last one here is are there any other elements that need to be mentioned or included in a post-approval study?

David?

DR. SEIFER: I just wanted to beg the last question.

DR. BLANCO: Go backtrack.

DR. SEIFER: If in five years, the failure rate looks greater than anyone expected, could then there be some kind of contingency plan to follow that for another X amount of time?

DR. BLANCO: We could recommend it, yes.

DR. SEIFER: So depending on the performance of the product.

DR. BLANCO: Yes, sir?

DR. LARNTZ: Are we saying if the product's really good, we want to penalize them to have them follow more?

DR. ROY: No, I think he meant if it was worse.

DR. LARNTZ: No, I thought he said if it was -- do I understand it? I'm asking if I understood that right. If it's really low, it's doing really well?

DR. SEIFER: No, no, no. If the people are getting pregnant using this product.

DR. LARNTZ: Oh, if they are?

DR. SEIFER: Yes.

DR. LARNTZ: Then you know there's a problem at five years.

DR. SEIFER: But then what do you do?

DR. LARNTZ: That's the information you'll have and that can be brought back. The FDA will have that information. They can give a report, do whatever they need to do with that information. Maybe they should tell me what they do, but what I would do is once you have that information, then you have to take action on that available information and decide based on if the rates are poor, then obviously someone needs to write a paper about it and it needs to be publicized, that kind of thing. I don't think you'd want to necessarily follow them more based on that. I think you've probably got the information you need.

So I did misunderstand you. I'm sorry.

DR. ROY: The private investigators would find each of us, bring us back here, and ask us why we approved this.

(Laughter.)

DR. BLANCO: Okay. I think we better get to voting pretty soon here.

Dr. Noller?

DR. NOLLER: Other elements of post-approval study needed. It would certainly be nice to know in actual practice what the failure to insert both devices at the first sitting would be. I don't know if that should be studied, you know, later as a retrospective study or if it should be part of the company's responsibility.

DR. BLANCO: I'm sorry. Let me interrupt you. The way it's written now and the way I think their proposal for the post-approval study is, they're going to follow the folks who already have it inserted. So what you're suggesting is that they need to gather further data on some of the -- I mean, I'm just clarifying. I don't disagree with it, but that they need to gather further data on the failure rates, especially maybe when it opens up to not so famous or whatever hysteroscopists. Is that what you're suggesting?

DR. NOLLER: I guess since the failure rate is so high, 12 percent, say, 8 percent, among experts, you know, if it's 20 or 25 or 30, who knows what it is, but let's just say it's 30 percent, I think we'd probably all agree it's probably not something that everybody should use. I doubt it will be, but I wonder if there shouldn't be some sort of surveillance of that.

DR. BLANCO: I think that's a good recommendation. I think it might even help them if the failure rate stays low in terms of their labeling and what it says.

MS. MOONEY: That may already be addressed, Dr. Blanco, in terms of the complaint reporting that --

DR. NOLLER: Think so?

MS. MOONEY: Well, I think that in that case,

the physician would probably be looking to have that device replaced or some sort of credit. So in my experience, those particular complaints, you do get pretty good reporting back from the sponsor.

DR. BLANCO: Well, I hate to put too much onus on the company, but I think that this is probably a big enough issue, that one is, that they need to look at that. I mean, maybe they don't need to look at it forever, you know. Some reasonable number to get a better gauge and also, like I say, it could improve and they may want to change their labeling or whatever.

So I think they need to not just rely on complaint reporting because a lot of docs will just say oh, I don't want to use it, and they'll not use it any more, and you may never get those reports. I think they need to make some effort to figure out with broader use what the failure rate is at initial insertion, but I could be convinced otherwise if somebody disagrees.

Dr. Brown?

DR. BROWN: Just one other thing that they might want to consider. I don't know if it would be necessarily a study but to keep some type of registry of users in terms of some of these other factors that were pointed out may be prognostic in terms of failure rate, such as age and ethnicity. You have that breakdown, but as

it comes into use in the general population, since we know that black women are basically, I guess, four times more likely, three times more likely to have failure with these other methods, it would be good if you could collect that data as it's happening so that it could be available.

DR. BLANCO: Any other suggestions for things that they should look at?

(No response.)

DR. BLANCO: Well, that ends the questions. If any of the panel members have anything else they want to bring up at this point with great urgency?

(No response.)

DR. BLANCO: No? Then we go to the final comments and what we do here is we open it up again to the audience and the FDA, then the sponsor, to make some final comments. This is not an interactive session or time for questions and answers, basically just a small amount of time to make a final statement.

Dr. Costello, are you comfortable with the statements that you've made?

MS. COSTELLO: Sure.

DR. BLANCO: You're okay? Do you want to make some other comments? Yes?

MS. COSTELLO: No, everything I said is fine.

DR. BLANCO: Okay. Dr. Costello is happy with

her comments. So we'll go ahead and go with the next one.

The next one that I have that has registered to speak before us is Dr. Amy Pollack, president of Engender Health. Please remember to introduce yourself and any conflict of interest.

DR. POLLACK: Hi. My name is Amy Pollack. I don't have any conflict of interest here, and I'm speaking to you as an obstetrician-gynecologist. I have a specialization in public health, and I'm the President of Engender Health and Engender Health is a not-for-profit organization working in the U.S. for the last 60 years and internationally for the last 30 in the field of family planning and reproductive health. We are most widely known for our experience and work with female and male sterilization in service delivery which is why I'm talking to you.

Bilateral tubal sterilization as provided today in the U.S. is considered both safe and highly effective. We all know this from years of clinical experience using different methods to access the tubes and then different methods to occlude them. Approximately half of the 700,000 female sterilizations performed annually in this country are provided as interval laparoscopic procedures. Those estimated 350,000 women choose for a variety of reasons to undergo a procedure that carries with it an estimated risk

that the procedure will lead to unintended abdominal surgery of almost 1 percent. That risk is not statistically related to the method of tubal occlusion. You probably heard about that this morning, but it is related to the necessity to enter the abdomen and to access the peritoneal cavity. This transgression alone represents the invasive nature of the currently available permanent sterilization methods.

In addition, female sterilization using both laparoscopic and minilap procedures are most often provided using local anesthesia in many other countries around the world. They are almost exclusively performed in the U.S. using short-acting general anesthesia. Data from the CREST Study cites the use of general anesthesia as a predictor of complications in women undergoing interval tubal sterilization.

Although there are many reasons to argue boldly for the development of and access to transcervical methods of sterilization, I would like to emphasize the two attendant risks described briefly above. Despite these risks, hundreds of thousands of U.S. women each year choose permanent sterilization. Many of those women might choose highly-effective temporary methods, such as hormonal implants or IUDs, if they were more readily available. But many of these women recognize the side effects of all of

the temporary methods as significant and as a disadvantage over permanent sterilization.

The recognizable risks of surgical sterilization and the side effects of the available temporary methods mandate the need for a transcervical option. After all, research to develop a safe and effective transcervical sterilization method has been ongoing for over 30 years. If we have now and I understand that there remain a few ifs here, a transcervical method that is well tested and is highly effective and safe to provide, one that can be provided without trespassing in the peritoneal cavity and that does not require general anesthesia, women in the U.S. should have access to that method.

In addition to that, I would like to urge the developers of Essure to be rigorous in their postmarketing surveillance, given some of the questions being explored here today, and to pursue simpler methods of placement of the device with the intent to market this device more widely on a global scale in places where permanent contraception is desperately needed by millions of women living in very low resource settings.

Thank you.

DR. BLANCO: Thank you.

The next speaker that I have that requested

time is Amy Allina, program director, National Women's Health Network.

MS. ALLINA: Hi. Thank you.

I am Amy Allina, and I'm the program director of the National Women's Health Network, which is a non-profit organization that advocates for national policies that protect and promote women's health and also provides evidence-based independent information to empower women in health care decisionmaking. We don't accept any financial support from pharmaceutical or medical device companies, and we're supported by a national membership of about 8,000 individuals around the country and 300 organizations. So I have no financial conflict of interest.

We've reviewed the information provided to the FDA regarding the Essure device and are here today to provide some comments on the questions before the committee, particularly as they relate to women's need for and ability to use this method of sterilization safely, effectively, and with long-term satisfaction, and I'm very happy that the committee's already addressed a number of the points that are in my comments. I think your discussion's been really interesting and very good today. So thank you for that.

Conceptus has provided a lot of detail about women's need for an expanded array of contraceptive choices

and Dr. Pollack also spoke about it. I won't repeat their arguments, except to say that the network agrees that existing options aren't adequate to meet women's reproductive health needs and that expanding the number of safe and effective contraceptive methods available would be a significant advance for women's health, helping to reduce unintended pregnancy and increase women's control over child-bearing and as a consequence other aspects of their health status as well.

That said, this is a new device and as you've discussed, there is not a lot of data available on its use. It's been tested in a few women and not for very long. We recognize the difficulty in doing clinical trials in this area and we have supported contraceptive approvals based on trials of this size and length and the focus of our comments today is on what women need to know to make an informed choice for Essure and especially on the question of how to convey to women the limits of our knowledge in light of the small number of women who have used it and the short time of the trial.

The network believes that the use of a written consent procedure for long-acting or permanent methods of contraception improves the likelihood that women and their clinicians will engage in the full discussion necessary to achieve informed choice, and we've asked the FDA to mandate

written consent for long-acting contraceptive methods in the past. In this case, the method in question is an alternative to a surgical procedure which requires written consent and we urge the FDA to mandate the use of a written consent procedure for Essure with the consent language to be approved by the agency and include similar topics and information to those proposed in the patient information booklet.

Providing patient information booklets can also be useful for helping women to understand the risks, benefits and consequences of their contraceptive choices, and we reviewed the proposed booklet, the language, and we have a few additions and amendments to suggest, some of which you've touched on, but we wanted to start by complimenting Conceptus on including language about women's right to be informed about other options and to change their minds about using Essure at any time without being required to provide explanation or reason. We were also pleased to see the acknowledgement in the patient booklet that Essure is a newer procedure and it hasn't been studied in as many women or for as long as other contraceptive options.

Our first and primary concern, I think, as you all have also focused a lot of your discussion, is on how to provide women with an accurate understanding of what's

known about the effectiveness of Essure. The statement that's currently included in the brochure in the Key Considerations Section, "if the Essure procedure is completed successfully, the one-year effectiveness rate is greater than 99.8 percent," fails to provide women with an adequate basis for understanding the limits of what's known and for comparing the device to other options where there is longer-term data.

Because of the small amount of data on Essure, it's difficult to compare its effectiveness to other methods that have been in use for many years, and we would like to see language included which explains something along the lines of, you know, while in a study of about 400 women, no one got pregnant in the first year. The study may have been too small to discover reliable effectiveness rate and to give some information about how effectiveness changes over time as seen, for example, in the CREST Study.

The patient information should also include a statement as you all have mentioned about the fact that some women who attempt to have Essure Inserts placed won't be able to use this method of sterilization, it might include a statement to the effect that in the trial, X percent of women who elected to use Essure underwent attempted placement but were not able to use the method, so that women know that going in before they decide to go

through any procedure.

In the Warning Section of the Safety Summary, Conceptus has proposed language concerning the unknown risks that may be associated with intrauterine therapies that use electrical energy and also the possibility that any intrauterine procedure could pose unknown risks and could interfere with Essure's effectiveness in preventing pregnancy, and we think these warnings should be explained in greater detail. The language should include information about the conditions which might make these procedures necessary, so that women have some understanding of what they really are agreeing to and those include endometriosis, fibroids, dysfunctional uterine bleeding, and the patient booklet should inform women that these conditions are not uncommon in women in their thirties and forties. This is also something that might be studied post-approval, what happens when those procedures are done in women using the device.

The Warning Section also includes language about the possibility that Essure may pose risks for women who choose to undergo in vitro fertilization and you all discussed this earlier. We do believe that this has the potential to be confusing regarding the reversibility of the device, but we also agree that it's something women need to know since some women will change their minds and

we wanted to suggest that there might be language to the effect, repeating what appears in other places in the booklet about the reversibility in that section about IVF, so that it would say something like the Essure procedure should be considered irreversible and you should only choose it if you're sure you don't want to have children in the future. If you change your mind in future years, which is not something that's in the IVF section right now, that it doesn't say if you change your mind, but to say if you change your mind in future years and decide to attempt to become pregnant using in vitro fertilization, you should know that the effects of Essure on the success of IVF in achieving pregnancy, the effects on your health, the health of your baby and the continuation of your pregnancy are all unknown.

The only other thing I wanted to mention was just on the question of the HSG versus pelvic x-ray or some other test. We recognize some of the reasons the pelvic x-ray might be preferable for women, for clinicians and also for the sponsor, but we don't have enough information about whether or reliably confirm the position of the device in tubal occlusion, and until studies have shown that pelvic x-ray is a reliable measure of these questions, we believe that an HSG should be required and also that the patient information booklet should explain that this test is

necessary to determine whether the Essure procedure has been successful and that the booklet needs to include a description of what's involved in an HSG and what that experience is like for women. I don't believe there's anything like that in there now since the sponsor wasn't suggesting that the HSG be required.

So my conclusion is just to say that in light of the need for expanded contraceptive choice and the desirability of making sterilization a safer choice for women, we support approval of the Essure device and we believe that if it's appropriately incorporated into the array of contraceptive options that are offered to women and adequately studied post-approval, it has the potential to advance women's health.

Thank you.

DR. BLANCO: Thank you very much for your comments, and I apologize for mispronouncing your name.

MS. ALLINA: That's okay.

DR. BLANCO: I still apologize.

All right. The last person that we have on the list that would like to speak before us is Wayne Shields, president and CEO, Association of Reproductive Health Professionals.

MR. SHIELDS: Hi, and thanks for the chance to talk to you this afternoon. I really appreciate it.

Again, the name is Wayne Shields, and I'm president and CEO of the Association of Reproductive Health Professionals. ARHP --

DR. BLANCO: I'm sorry. Before you start, make sure that you say something about conflict of interest.

MR. SHIELDS: Yes, I'm about to do that.

DR. BLANCO: All right.

MR. SHIELDS: We receive support from our individual members and we receive foundation grants. We also receive support from restricted educational grants from companies, and we have in the past received that kind of support from Conceptus. So I wanted to be sure you knew that.

I represent about 2,400 health care providers and those include not just physicians but nurse-practitioners, nurse-midwives, and physician assistants, all the advanced practice clinicians, some educators and scientists, but they're all directly involved in the practice of women's health and reproductive health. I also represent a larger constituency of 15 to 20,000 primary care physicians and advanced practice clinicians who regularly participate in our educational programs that we develop. Our members work in both the public health sector and in private practice. So they're really basically in all types of environments.

ARHP's mission is education and we've been educating health care providers and the public on reproductive health issues since 1963. So it's almost our 40th year. We work closely with other organizations. My friends and colleagues, Amy Allina and Amy Pollack, are in the room. We've worked with their organizations and many others. All of the acronyms that you can possibly imagine in Washington, D.C., we've worked with them at some point.

The reason I'm here is that although ARHP has addressed many reproductive health topics through our accredited education programs over the years, much of our focus has been on contraception and I'm sure you can imagine why, particularly with health care providers in need of this kind of information. ARHP places a very strong emphasis on provider education, provider training and particularly on patient counseling. Those are what we see to be the most important, I'm sure you do, too, the most important ingredients of safe and effective contraceptive health care, and we also view communication between the health care providers and the patients as key and an essential part of better health care.

Also because every woman's and man's needs are unique, ARHP supports the availability of as many safe and effective contraceptive options as possible, and we believe this is critical for the good health care of women and men

in the United States, and it's key to a healthy functional health care system here in the U.S.

Many women prefer, of course, reversible methods of birth control because they want the option of having children at a later time, and it is a huge counseling issue. It's an important one. Others have preferences for things that are more "natural," but in the U.S., there's just the option right now of one type of sterilization option, and women who choose sterilization do choose tubal ligation, but I'm here to say that we're very pleased that women have the potential to have access to a new, safe, effective sterilization option in the U.S. We think this is a very positive development, and at our organization, we're particularly pleased at the care that the manufacturer, Conceptus, has taken to thoroughly study this new method and I know we've talked about that today, but also to carefully focus on provider training and education about the insertion. You witnessed that earlier. Our impression is that they have done a very good job thinking about this at length and believe me, we've talked to other organizations and companies who haven't had this type of depth of thought, and it's definitely appreciated by our members and by our board.

The other part that's important to us at ARHP is that Conceptus seems to have recognized the critical

importance of patient counseling in making decisions about permanent sterilization, and of course, to Amy Allina's statement about including information about IVF in the labeling. Women do change their minds, and it's critical that women do have information about what it is they're about to decide in an adult conversation with their health care provider, and to us, this is critical, and I'm sure it is to you all as well.

I was very pleased and surprised, as was our board, to find that Conceptus had thought about this in length and that their interest in patient counseling matches that of ARHP. So we're very pleased about that, and I'm very convinced at this point, which is I think a good thing and it's not that common, about this company's commitment to very thorough appropriate training and also to patient counseling and that's key, and I'm glad to see that and I wanted to share that with you, and thank you for allowing me to comment.

DR. BLANCO: Thank you very much.

I thank all the audience for your participation.

Now, is there anyone else in the audience who hasn't signed in that would like to make a comment?

(No response.)

DR. BLANCO: Next is the FDA, a member of the

FDA, for some final comments at this point. No comments from the FDA at this point?

MS. BROGDON: No. We have no comments.

DR. BLANCO: No comments. That's very politically correct.

All right. Then it's the company's opportunity to come forth and make some comments at this point.

MS. DOMECUS: Thank you for the opportunity to provide a few comments on the discussion that ensued since our presentation. I just wanted to address a few points mostly for clarification.

First, of course, I'd like to address the issue of x-ray in lieu of HSG. I wanted to provide a couple of clarifications. Dr. Brown, I think you had a question about why our training program didn't provide interpretation of x-rays to the radiologists, and I wanted to clarify that our plan was to train the gynecologists who perform the procedure in the appropriate interpretation of x-rays and that we were not recommending that the radiologists do that interpretation.

Second, I just wanted to clarify that the x-ray at three months was being suggested as a first step and that if there were any suspicious findings noted on x-ray, that then those subset of patients would undergo an HSG. If there was clearly unsatisfactory device location, those

patients would not undergo an HSG but would be told to use alternative contraceptive methods. So some patients would undergo an HSG if the x-ray showed suspicious findings.

I think I heard in the discussion today but I just wanted to reiterate that all of the unsatisfactory device locations that we found in the trials could be detected on pelvic x-ray alone. It seemed to me, though, that the discussion centered around the 4 percent patency rate, and so I wanted to highlight a point which I believe the industry representative made that I think is of critical importance, and I wanted to just read two sentences here from the PMA just to address this point.

Bruce, et al., reported a patency rate of 16.7 percent in a study of 54 tubal ligation patients followed for an average of 4.5 years and cited literature references for a total of over 1,000 patients followed for three months where the average patency rate was 3.2 percent. It should be noted that the pregnancy rates in these studies do not equal the patency rates noted. Therefore, it has been reported in the literature, and I quote, "Although there may be failure of absolute physical occlusion of the tubes, this cannot be directly equated with failure of sterilization."

I would like to tie that comment to the histology data that was presented earlier where Dr. Wright

showed that not only was the tissue response occlusive in nature but that also there was consistent loss of normal tubal architecture in all specimens evaluated, and I also would like to remind you of his comments about the amount of tubal occlusion and damage that he's seen in our histology specimens as compared to that seen in specimens from ectopic pregnancies.

I wanted to provide a couple of clarification points on training. I just wanted to clarify that the preceptoring for five cases is what we expect to be the average. It's not a minimum, that we will not sign people off until they have demonstrated competency. So I just want to be clear, we expect it to be an average of five based on our pivotal trial data, but it's not a minimum of five.

I also wanted to clarify the comments about training and local versus general anesthesia, and I'm reading from our labeling. We actually recommend that local anesthesia be used. What we say is local anesthesia is the preferred method for implantation of the Micro-Inserts. So we actually recommend that in the labeling.

I also think there's a lot of discussion around the concern about how generalizable the placement success rates were in the pivotal trial to the general population, and I just wanted to remind the panel about the data that

we do have in that regard, that we're not without data to speak to that. I presented a slide earlier this morning that showed the baseline, just an average of four procedures per physician with our commercial training program to date, that we're already having success rates that are very close to those in the pivotal trial. So we do have data to speak to how generalizable this might be.

I'd also like to remind the panel of the figure we presented earlier this morning, that when looking at placement failures that were evaluated by HSG, that 83 percent of them were found to have proximal tubal occlusion. So placement failure isn't just a factor of physician experience or learning curve, it's also an anatomy issue.

There's also some comments or suggestions to have an implant card or patient ID card, and I just want to clarify that that's already been proposed in the PMA. We did so in the clinical trial as well and the back of the card carried some statements about not having data on the future procedures, such as IVF, intrauterine procedures, et cetera, and so we are proposing to do that in the commercial setting as well.

Dr. Shirk, you also raised some issues about unilateral placement and what we would suggest in that regard. In the protocol, we allowed patients the

opportunity to come back for a second placement procedure after first undergoing a follow-up HSG since the likelihood of PTO was probably increased in the patients who had placement failure, and many patients did elect to undergo a second placement procedure and were successful, and so we'd be happy to include our protocol recommendations in the labeling as well regarding patients that achieved unilateral placement at first visit.

There was also some discussion about the label containing cautions about lack of data on IVF, and I just wanted to clarify that both the physician and the patient labeling do have that language and the physicians labeling has it in the Warnings Section and the patient labeling discusses it under the section on Procedures that we don't have safety and effectiveness data, and contrary to the prior speaker, I wanted to point out that these bullet points in both the physician and patient labeling, that bullet point is right next to the bullet point on reversibility and how we don't have any data on the success of the reversibility.

I also want to comment about the postmarket surveillance and the five-year follow-up, and there seemed to be some concern that we might have decreases in pregnancy rates and if so how would that be known and how would that be communicated, and I just wanted to clarify

that, you know, once we have the next year failure rates established, we will be submitting that to the FDA and certainly if there is any change, we would be required to update our labeling. We wouldn't wait till five years to then let patients know that there was a change in the failure rate.

I think that was all the clarification comments that I had.

DR. BLANCO: Thank you very much.

All right. Now we come to the voting on panel recommendation options and I'm going to go ahead and read the options for premarket approval applications.

"The Medical Device Amendments to the Federal Food, Drug and Cosmetic Act (the Act), as amended by the Safe Medical Devices Act of 1990, allows the Food and Drug Administration to obtain a recommendation from an expert advisory panel on designated medical device premarket approval application (PMAs) that are filed with the agency. The PMA must stand on its own merits and your recommendation must be supported by safety and effectiveness data in the application or by applicable publicly available information. Safety is defined in the Act as reasonable assurance, based on valid scientific evidence, that the probable benefits to health (under conditions on intended use) outweigh any probable risks.

Effectiveness is defined as reasonable assurance that, in a significant portion of the population, the use of the device for its intended uses and conditions of use (when labeled) will provide clinically significant results.

"Your recommendation options for the vote are as follows:

"Approval, if there are no conditions attached.

"Approvable with conditions. The panel may recommend that the PMA be found approvable subject to specified conditions, such as physician or patient education, labeling changes, or a further analysis of existing data. Prior to voting, all of the conditions should be discussed by the panel.

"Not approvable. The panel may recommend that the PMA is not approvable if the data do not provide a reasonable assurance that the device is safe or if a reasonable assurance has not been given that the device is effective, under the conditions of use prescribed, recommended, or suggested in the proposed labeling.

"Following the voting, the chair will ask each panel member to present a brief statement outlining the reasons for their vote," and I would just add that the vote is vocal and individual by person as we go around.

Just from prior experience, I'd like to suggest that we basically see if anyone is interested in providing

a motion for approval or not approval and then depending on how those go, we'll see the approval with condition. So at this time, I will entertain a motion, if anyone would like to make it, of approval with no conditions.

Dr. Shirk would like to make the motion. Is there a second to that motion?

DR. SHARTS-HOPKO: Second.

DR. BLANCO: Second to that motion.

Is there any discussion at this point? I'd like to open up the discussion. We put a lot of conditions already that we discussed. So I'm not sure that we can add those or that they will be there. If we approve it without conditions, it's done, and they don't have to change a thing. Okay? So I'm not sure that that's -- that wasn't what I was searching for really.

(Laughter.)

DR. BLANCO: But I'm not sure that that's where we want to go. Let me just put it that way. If we want all these labeling changes and we want the issues that we have all discussed, then we need to add those as conditions. Okay?

Any other discussion anyone else would like to say anything?

(No response.)

DR. BLANCO: Then I'll ask the voting members

to vote on the motion on the floor. We'll start with you, Dr. Shirk, over in that area.

DR. SHIRK: I guess at this point, I think the company's aware and responsible and I guess I would vote for approval.

DR. BLANCO: Okay.

DR. LARNTZ: No on the motion.

DR. BLANCO: Dr. Roy?

DR. ROY: No on the motion.

DR. BLANCO: Dr. O'Sullivan?

DR. O'SULLIVAN: I abstain.

DR. BLANCO: Dr. Sharts-Hopko?

DR. SHARTS-HOPKO: Despite seconding it, no to the motion.

DR. BLANCO: Thank you.

DR. BROWN: No on the motion.

DR. BLANCO: Dr. Brown.

The chairman doesn't get to vote, unless there's a tie. So we'll keep going to the right.

DR. SEIFER: No on the motion.

DR. DUBEY: No on the motion.

DR. NOLLER: No on the motion.

DR. BLANCO: The results are one yes, seven nos, one abstention. The motion does not pass.

I may be getting into trouble again, but this

time, I'll ask to see if anybody wants to make a motion for not approving the PMA flat out.

(No response.)

DR. BLANCO: Okay. No motion.

Then I will at this point entertain a motion for approval with conditions and then we can begin listing conditions.

Dr. Noller?

DR. NOLLER: I move that it's approvable with conditions.

DR. BLANCO: Any second?

PARTICIPANT: Second.

DR. BLANCO: I hear a second.

Now, what we need to do at this point is we need to go through the conditions, get a vote of general consensus at least on each of the conditions, an actual vote if there's controversy and then we will vote on the entire thing again. Okay? So anybody care to lead off with some of the conditions we'd like to place, and if you can, can you do them in order of the questions, if you can, or if not, whatever order. Sorry.

Go ahead. Dr. Brown?

DR. BROWN: One condition would be that HSG be required as it was done in the pivotal study as opposed to substituting the plain x-ray.

DR. BLANCO: So you would like the study to be done --

DR. BROWN: The commercial use to reflect the conditions of the study.

DR. BLANCO: Okay. Do you want to make any suggestion that if the company provides data, it should be brought to use something else, if effective should be brought forth and reconsidered?

DR. BROWN: Yes, absolutely.

DR. BLANCO: Okay. Any comments on that condition? Anybody else wants to amend it or add anything else to it?

DR. SHIRK: My question would be, would ultrasonic HSG be as good as regular radiographic x-ray?

DR. BLANCO: Well, we don't know that. So I don't think we can recommend that.

DR. SHIRK: Okay.

DR. BLANCO: I think that would not go over. I think that the best that we can do is that at the present time, they replicate their study for commercial use and that they be encouraged to gather further data on optional ways of doing it and bring that data forth to be able to change that recommendation. Is that fair enough?

Is there general agreement on that statement or should we take a hard vote? General agreement? Everybody

shake their head. Yes, there seems to be general agreement. So we'll move on. Okay?

Any other recommendation? Dr. Brown, since you started, we'll just go with you.

PARTICIPANT: The hypervolemia.

DR. BROWN: Oh, the qualifications of the training, that the company provide some basic qualifications to include a statement about general hysteroscopic proficiency.

DR. BLANCO: I think, remember, when we were talking about it, we said knowledgeable hysteroscopists in the discussion, and maybe we need to bring it up again and see if we need a hard vote on it, was the issue of diagnostic versus operative hysteroscopists.

Dr. Noller, I think you brought up something about that, and Dr. Shirk, you guys want to address that? Which way do you want to see it?

DR. SHIRK: I think just a general statement is fine. I don't see that we need to differentiate between diagnostic or operative.

DR. NOLLER: I agree.

DR. BLANCO: You agree? All right. Anyone else disagree? Anybody else wants any stronger language or recommendation?

(No response.)

DR. BLANCO: Then as I have it now, it is recommended that the company in their training program put something to the effect that one needs to be a knowledgeable hysteroscopist in order to be able to utilize this device. Is that acceptable to most people? I'm sorry. Did someone have a hand up? No? Okay.

All right. Any other conditions?

DR. NOLLER: I have one.

DR. BLANCO: Please. Go ahead.

DR. NOLLER: I would like to see the labeling for both the physician package insert and the consumer prominently include the fact that approximately 10 percent of first placements, first-time placements are unsuccessful.

DR. BLANCO: Any comments on that? Everybody's in agreement with that? Why don't we tackle other labeling issues, if we could, while we're at it? Anybody want to bring up any other labeling issues?

DR. BROWN: That there be stronger -- I'm sorry.

DR. BLANCO: No, go ahead. Go ahead, Dr. Brown.

DR. BROWN: That there be a stronger statement in the physician labeling about the age of the patient and the correlation between young age and patients changing

their mind and just emphasizing that the physician needs to be aware in their selection of patients, they should be highly selective of patients who are sure about their decision and in the patient labeling maybe even stronger language about the irreversibility of -- emphasizing more that there is no known way to reverse this procedure. I think that is a true statement.

DR. BLANCO: Okay. Anybody else want to refine it, add anything to it, something along those lines?

(No response.)

DR. BLANCO: All right. Go ahead.

DR. SEIFER: For the physician labeling specifying a consistent time before they consider to stop the procedure.

DR. BLANCO: I'm sorry. Wait a minute. Let me clarify.

DR. SEIFER: Whether it be 20 minutes, 30 minutes in terms of the duration of the first attempt. Also, some specifics with regard to perhaps the fluid deficit. Somebody from Conceptus said 1,500. That's what they're teaching their classes with. I know there's disagreement about that amount, but I think it should be specified.

DR. BLANCO: Okay. Specify the amount. You want to make the amount 1,500 milliliters?

DR. SEIFER: That's what they're teaching. I'd prefer it, yes.

DR. BLANCO: Okay. Anybody have a problem with that?

DR. ROY: But I don't think that's fluid deficit. That's total fluid use.

DR. SEIFER: Yes.

DR. BLANCO: Well, I think Dr. Shirk had mentioned earlier three liters. So if the company was 1.5 liters, that sounds to me like --

DR. SHIRK: That's if you look at a drug and what dose's limiting factor is half-lethal dose and so, I mean, three liters of fluid is not going to drown somebody.

DR. BLANCO: So 1.5 is less likely to --

DR. SHIRK: One point five is well within the safety range.

DR. BLANCO: Anybody else? Yes, sir?

DR. DUBEY: Yes. The success of this device, when it puts on the label like 99.8 percent, should be defined with number of patients tested for limited number.

DR. BLANCO: And I think it should be clarified, 99.8 percent, I think, is --

DR. DUBEY: Based on like 400 cases, 500 cases.

DR. BLANCO: Yes, I'm not sure what I would put in there, but something that's more applicable to patients

and that maybe does have that number in there in terms of the success rate of the procedure.

All right. Any other comments on labeling?

DR. SHARTS-HOPKO: Caution with metal sensitivities.

DR. BLANCO: Metal sensitivities. Actually, let's broaden that. Metal sensitivities and the electrocautery issue and there was one third one. What was the third one that we discussed?

DR. ROY: Pregnancy IVF.

DR. BLANCO: Right. Thank you.

Okay. So something to address the issue of metal sensitivity and no longer use of electrocautery and subsequent pregnancy.

DR. O'SULLIVAN: I might add that every effort should be made, in fact it probably would be better to put it on the product labeling, that these should be done only in the proliferative phase, ideally in the first 10 days.

DR. BLANCO: Okay. Everybody agrees with that?

PARTICIPANT: Yes.

DR. BLANCO: Okay. Go ahead.

DR. SEIFER: Is there a way to put in the labeling something that will help with the follow-up of these patients so that Conceptus has an easier time keeping tabs on these patients for the five years that they've

agreed to follow them? In other words, motivate the consumer who's getting this product with regard to the importance of participating in the follow-up with this company?

DR. BLANCO: What did you want to say?

DR. SEIFER: An incentive is always good. Disincentive is probably less.

DR. LARNTZ: I mean, these patients who are being followed for five years are already implanted.

DR. BLANCO: Right. They're going to follow the ones that are already in there.

DR. LARNTZ: That are already implanted already.

PARTICIPANT: (Inaudible.)

DR. LARNTZ: Right. So I don't think that applies.

MS. LUCKNER: You can shape patient expectation by putting in the patient information brochure how helpful it will be for their own women's health to notify their provider of certain conditions and that you'd like it for about five years.

The only other thing I haven't heard discussed is the issue of informed consent. One of the last speakers talked about consent. There is a difference between informed consent and consent. Are we going to make a

comment about that?

DR. BLANCO: Well, I had it written down, and actually it never even occurred to me, and I'm glad the speaker brought it up. It never even occurred to me that it wouldn't be written consent for this. I mean, maybe I'm making a big deal about that, but to me, it just seemed that was kind of like a given.

MS. LUCKNER: But written consent does not imply informed consent.

DR. BLANCO: Well, what would you like to be sure that it is informed consent?

MS. LUCKNER: Use the word informed consent.

DR. BLANCO: Okay.

MS. LUCKNER: Governed by many places by statute.

DR. BLANCO: What about written? Do you agree with that?

MS. LUCKNER: Yes, definitely.

DR. BLANCO: I hear some yeses. Okay.

DR. BROWN: I'm sorry. I have a question about that. So are we saying that the company must provide a standardized written consent as part of the package or are you saying -- because obviously patients who undergo this are going to need to undergo, unless it's in a private office and you don't have to do that, but you would be

cited if you performed the procedure without informed consent, but certainly if it's done in a hospital setting, the physician who's doing it will have to have written and documented that I had informed consent.

I thought the speaker was specifically referring to some type of standardized language and something that is provided by the company that --

DR. BLANCO: Well, I think that's what you're saying because what consent you're going to get, if you take them in the hospital, is going to be an OR consent. I'd like to hear from the industry representative, but I don't think it would be a major onus on the company to produce what represents an informed consent. They've already done a lot of that in the PMA that's submitted, I think a lot of the information, and then just have that available for the physicians to use on their patients. I don't think we want to make the onus that it's the company's responsibility to make sure every physician uses it. Lord knows we can't get physicians to do anything. So I wouldn't go that far, but at least they can provide it so that if the physician doesn't use it, it's really the physician who's at fault for not doing the appropriate thing.

DR. BROWN: Could I just make one suggestion? It's part of what I was going to finish saying. I mean,

many studies have shown that the value of written informed consent is very, very low, and we were talking about women's preconceptions and miscommunications. So I was going to suggest that maybe the company, as long as they're doing this, might want to go ahead and make a video or some type of other mode that you could use to inform the patients, besides just the written word, a CD-ROM that the person could put in their office and show to the patients before they have the procedure. Something like that might be very helpful as another type of means of getting across the informed consent.

MS. MOONEY: Yes, Dr. Blanco, I agree. I think it's reasonable to ask the company to recommend a language for informed consent and then people will apply that and modify that as fits their practice and that it would be the onus of the physician to ensure that that's done.

DR. BLANCO: Now, what about educational materials? That's what you're really saying, Subir, whatever. How do people feel about that? What do they think?

DR. ROY: Well, you're going to have, I suppose, a patient information --

DR. BLANCO: Booklet?

DR. ROY: -- booklet. I think the video is very good, and then you have also a written informed

consent that repeats it for the third time, and then it should be an informed consent, informed written consent. So I think all three are certainly suitable. How else are you going to convey a lot of this information that we've been talking about?

The other thing I'd do is once they get it in, I'd give them a card that contains this information as well, so that if they were to have a surgical procedure or something like that, they could pull it out and explain it to the appropriate clinicians.

DR. BLANCO: Yes?

MS. BROGDON: Dr. Blanco, I think it's fine that the committee has recommendations to the sponsor for wording for informed consent written documents. However, it would be impossible for FDA, I think, to institute that as a requirement on this or another sponsor. It's almost impossible for us to require this because we can't enforce it. So you can make whatever suggestions you wish as a suggestion, we just can't require it.

DR. BLANCO: Well, I don't think the requirement was that every patient have it because just like I said, that's really more the physician. The only suggestion of requirement was that the company provide it for the physicians to utilize with their patients. I don't think --

MS. BROGDON: Yes.

DR. BLANCO: That was the point I was making, was addressing. I think we can put the onus on them that everybody has it. They just provide the materials.

MS. BROGDON: That's fine.

DR. BLANCO: Then it's up to the physicians to utilize it. Okay?

All right. Everybody's in agreement what we've said so far? All right. Any other problems? Any other suggestions that we want to make? Let me go back to one. We talked about recommended length and limit of 1,500 milliliters. I also had a size of scope as a small scope that was brought up during the discussion. Do we want to address that or just leave it up to the person? I think I would leave it up to the person because you may need different scopes for different people. It was brought up.

DR. SHIRK: The problem with that would be a lot of hospitals, if it's done in the hospital setting, already have scopes of greater diameter that would force, if we put a limit on size, it would force them into buying new equipment.

DR. BLANCO: So throw that out. Everybody okay with that? Okay. Yes?

DR. NOLLER: I just reviewed the patient information labeling to make sure, but there's no mention

of what to do if you think you might be pregnant, if you miss a period, because if that happens, the risk of ectopic pregnancy is probably high. I think it should be mentioned in there.

DR. BLANCO: All right. So if miss a period instructions, recommended procedures if you miss a period.

DR. NOLLER: Talk to your doctor, get a pregnancy test, that sort of thing.

DR. BLANCO: Okay. All right. The other one that I have written down is fallback plan if you run into the failure rate. Okay. Does anybody want to make it more specific than that or is that general enough? They've heard everything we've said. Okay. So fallback plan.

DR. O'SULLIVAN: You're going to ask the company to require that?

DR. BLANCO: No, we're just going to make it in the labeling. We're talking about labeling right now that they suggest. I think the way we worded it was when we discussed it was that the company should make a suggestion that if there is this failure rate and in case there's a failure, you should have discussion with your physician as to what you're going to do if he or she's unable to insert the devices bilaterally. Is that fair enough? Okay. I just like to shorten things. Fallback plan.

Anything else that anybody wants to add?

DR. SEIFER: There was a question about if there was tubal pathology before putting this device in, if --

DR. BLANCO: We didn't address that a lot other than mention it.

DR. SEIFER: Yes.

DR. BLANCO: We didn't discuss that a lot, whether there might be a higher rate of perforation, pain with small hydrosalpinx, something like that.

DR. SEIFER: Or formation of a cyst, hydrosalpinx, after placing that because of distal and proximal obstruction.

DR. SHIRK: I think it could be in the informed consent as a possibility, but I don't know how we would predetermine that a patient's got, you know, distal tubal disease.

DR. BLANCO: Well, I'd hate to drop back into a major discussion, but you could make it an exclusion criteria where if they've had a history of pelvic inflammatory disease, not necessarily recommending that. I'm just saying it would have to be something very broad at that point.

The pleasure of the panel? Do we want to address it, say anything about it?

DR. O'SULLIVAN: There's another issue

regarding pelvic inflammatory disease. First of all, in the study, they did require that the patient subsequently deliver if she had a history of pelvic inflammatory disease, but I think the other issue is pelvic inflammatory disease is very subtle and quiet and you don't know anything about it, such as associated, let's say, with chlamydia, and that's not going to help you. It's not going to get you off the hook. I mean, you might want to make that a requirement, but it's got to be understood that you may not have had a history of it but still have.

DR. BLANCO: So what would you recommend? How should we address the issue of PID? We didn't really talk about it a lot. That's a good point.

DR. SHIRK: I just think if they wanted to put it in informed consent, it would be fine, but I think it would be difficult to put it in the labeling for the physician. I mean, I don't know how you determine that. I mean, 65 percent of women that have endometriosis have been diagnosed as having PID at least once. I mean, that's a disease that has nothing to do with pelvic infection. I mean, I don't think our criteria for PID are good enough. I mean, in the best hands, you're only going to be right on a diagnosis of PID at 60 percent of the time. That's already documented.

So I think it's a difficult issue to tackle. I

think that it might be part of the informed consent that if you have previous tubal disease, it may create complications, surgical complications, in the future, but I don't know that it should be in the labeling per se.

DR. BLANCO: Well, what about should we recommend that the company look at that issue? They're going to be looking at their patients, but we also had mentioned some things that they might want to look at in a post-approval study. I mean, do they need to look at that and have some better idea of what this device is going to do in people with PID or even just as they -- you can look at it the other way around. If they get patients who develop significant infections after insertion of the device to try to ascertain whether they might have a history of salpingitis before or some evidence of it that might have been the reason why this happened?

DR. SHIRK: And then are we going to recommend that they have a post-approval databank for all patients having the procedure done?

DR. BLANCO: Well, no.

DR. SHIRK: I mean, that's what you're suggesting.

DR. BLANCO: No, no. We talked about a registry. I think Dr. Brown mentioned a registry of complications, looking at those. That's all that I was

bringing up, not keeping track of every single patient that ever has it put on.

DR. NOLLER: Question.

DR. BLANCO: Yes, go ahead.

DR. NOLLER: For insertion of IUDs, you're supposed to have a negative chlamydia and GC test before you insert it. I just quickly looked through here. I didn't remember it and I didn't find it just now. If it isn't in there, I would think that wouldn't be a bad idea. We didn't discuss it before. I'm sorry.

PARTICIPANT: It is in their study.

DR. NOLLER: It was in their study but in their recommendations for use training, I didn't see it. Is it in there? Does anybody remember? It just seems a reasonable thing to do. It says no recent or current pelvic infection and in their studies, they said they did lab tests, but I don't see it for a routine recommendation in there.

DR. ROY: But the culture or PCR for chlamydia could be negative, but they could have had prior --

DR. NOLLER: Correct.

DR. ROY: -- exposure with a high titer and unless you did something else, you might not know that the distal oviduct was closed.

DR. NOLLER: It's two separate issues, yes.

DR. BLANCO: Yes. One issue is where there's some baseline or some history of salpingitis, and I think the impression I was getting from most people is probably other than recommending that they realize this and if they start getting patients with infection, reports of patients with infection, that they need to take a look to see whether it may be that this device is inflaming, you know, some old infection, but that's one issue.

The other issue is the issue of do you want to -- Gerry, when you're going to do a hysteroscopy diagnostic with therapeutic on someone for whatever, do you get a GC and chlamydia culture before you do it on the patients?

DR. SHIRK: Not routinely, no.

DR. BLANCO: What do you think? What's your sense of the countrywide utilization of that?

DR. SHIRK: I don't think it's routine for hysteroscopy.

DR. BROWN: Or for endometrial biopsy.

DR. SHIRK: Or endometrial biopsy. I mean, I just don't see it. I mean, obviously if you're putting in a device, I suppose, like an IUD, that's a new indwelling device, then it's obviously important.

DR. BLANCO: Well, so is this, though.

DR. SHIRK: So I have no problem culturing them or recommending that they do that. I think that's

reasonable. The hysteroscopic procedure itself, I don't see it as an issue.

DR. SEIFER: I think it's probably regional. I mean, some parts of the country, I think when you do an initial work-up, you're doing cultures on patients.

DR. BLANCO: Dr. Noller, what do you think?

DR. NOLLER: I really don't know. We don't have data to make a rational decision. It is an implanted device. It's different from a diagnostic procedure that has a beginning and an end quickly. This will be there for years, but I don't know if it's a risk or not.

DR. BLANCO: What do you think?

DR. SEIFER: I think a culture's relatively cheap to do and it's usually done before you can do a hysteroscopy anyway because it's part of your initial work-up of the patient. So particularly with the new device, such as this, I would support doing it.

MS. MOONEY: Dr. Blanco, maybe since we're on the fence on this, one option would be in the labeling to say "recommend" rather than "require." It calls the clinician's attention to that, but you give some option based upon that individual patient's situation.

DR. BLANCO: Yes, and I think the other thing is that it also depends on the individual. I mean, I think if I were still back in Houston at LBJ with an inner-city

population, I'd probably want some cultures or DNA for those. I think in Iowa, maybe you don't need to do it so much. Those cornfed girls up there.

(Laughter.)

DR. SHIRK: I mean, obviously it's a patient population.

DR. BLANCO: Dr. Brown?

DR. BROWN: I would just point out that the current labeling does say contraindications pretty clearly, active or recent pelvic infection and untreated acute cervicitis. I mean, I think it's a matter of semantics if you wanted to add on to that cultures, but in the physician training module, they clearly say negative pap smear, negative GC and chlamydia. I don't personally think it's necessary to add anything else, but I think it's pretty clear, what's already in here, that's how to handle it.

DR. BLANCO: Happy with that?

PARTICIPANT: Yes.

DR. BLANCO: We'll forget that.

All right. The only one that I have written down is the five minimum, the proctored, as part of the training. Anybody want to address that? I think everybody kind of liked five, I think, except for you. Okay. So we'll put the five. Anybody against that?

DR. BROWN: I'm kind of against it, because I

think, you know, if somebody is already a very accomplished hysteroscopist, it's probably going to frankly take them about two seconds to do this and they may not need to have five proctored, and as they said, it may take more than five in some people. So I would rather leave it loose, frankly, and then also for the future in terms of medical education. So I think it's better to leave it open.

DR. BLANCO: All right. You still have faith in your fellow physicians. It's nice to see that.

(Laughter.)

DR. BLANCO: All right. How do we want to do this? It sounds like there's enough difference of opinion here, I'd like to take a vote on suggesting either a minimum of five or an average of five which is how they placed it.

DR. NOLLER: Point of order, point of information. Once this is out there, if you get privileges to do this or if you have a private office, you're going to do them, you know, you're able to do it with zero proctored insertions. So you know, whatever we put as the recommendation that in fact people maybe to get credentialed to do it in their hospital have to have five, if it says five, but there will be an awful lot of people doing them with zero.

DR. BLANCO: Well, all we can do is have faith

in the fellow physicians.

MS. BROGDON: Dr. Blanco, I don't know if anyone asked the firm if they have plans to not ship the device unless people are signed off. You might want to find out what their proposal is.

DR. BLANCO: Would you all care to answer that? Don't put the five because they said not, they said an average of five. So let's say, are you planning on shipping the equipment before you have some knowledge that this person has had some experience with the device, whatever that experience turns out to be?

MS. DOMECUS: We won't ship devices to physicians who haven't completed the training program, unless there is a preceptor going with those devices.

DR. BLANCO: Okay. So then it does become important to say average or minimum.

Okay. Any more discussion to an average or minimum? All right. Well, I think we better take a vote on this one. Which way would you like to see it? Subir, which way do you want it, and we'll vote that up or down, and it's my fault.

DR. ROY: Until the physician has demonstrated competency.

DR. BLANCO: Okay. Anyone want to second that?

DR. BROWN: Second.

DR. BLANCO: Okay. Second. Any further discussion? Okay. Let's start out over on this end.

DR. NOLLER: Aye.

DR. DUBEY: Yes.

DR. SEIFER: I vote no.

DR. BROWN: Yes.

DR. SHARTS-HOPKO: No.

DR. O'SULLIVAN: Abstain.

DR. ROY: Yes.

DR. LARNTZ: Yes.

DR. SHIRK: Yes.

DR. BLANCO: Please do say it into the microphone. This is for posterity. I mean, that's okay this time but for the future.

DR. SHIRK: Yes.

DR. BLANCO: Six yeses, two nos, one abstention. So the recommendation will be as worded by Dr. Roy and I won't try to repeat it but it's in the record. Okay?

All right. Okay. Anything else that we need to include as a condition or that we would like to include as a condition? Anyone else? Going once, going twice. Okay. This is what I was looking at, you know. We agreed with the five-year postmarket analysis of the patients that are currently enrolled, and Dr. Noller, I think it was you

that brought it up but if not, that's okay, I'll take care of it.

Any further assessment of the failure rate for placement? Do we want, once it's out in the general marketplace, and this is what I was talking about, a registry of failures to try to understand the rate a little bit better once it gets out into the community? Anybody want to address that?

DR. ROY: Well, don't you have to have a registry of users before you can have a registry of failures? I mean, you could have the other, but it's sort of worthless.

DR. BLANCO: You wouldn't have any denominator. Anybody, how strongly do you want to look at this?

DR. O'SULLIVAN: Well, they're going to have a registry of users. I mean, that's going to be easy enough for them because they're the ones that ship them out. They know they can't go out without a proctor. Okay. So they're going to have a registry of users.

DR. BLANCO: Okay.

DR. O'SULLIVAN: And then, I think that the next issue is follow-up from the user, if he has difficulties getting them in what they were.

DR. BLANCO: Because basically what you're saying is that when they ship them out, when they have a

preceptored user, so that they're shipping regular numbers of these, that they get some sort of report back from their user in terms of how many failures they had. That's probably not that difficult.

DR. O'SULLIVAN: And it's easy enough because then they don't ship out again until they get it back from them.

DR. BLANCO: Power.

DR. O'SULLIVAN: Yes.

MS. MOONEY: Dr. Blanco, I think maybe the recommendation I would make would be to communicate to the sponsor and for the record that we want to have some way of assessing the failure rate, but I think it may be most prudent to let them work that out with the FDA as far as the actual method.

DR. NOLLER: Yes. I agree with that.

DR. BLANCO: Very nice. Thank you.

Is that all right with everybody? All right.

MS. BROGDON: Dr. Blanco?

DR. BLANCO: Yes, ma'am?

MS. BROGDON: I think we would like probably a clearer recommendation on whether the panel is recommending that there be a new postapproval study as opposed to continued follow-up of the subjects for five years.

DR. BLANCO: All right. Well, the panel will

correct me if I'm wrong, but I -- no. The panel would like the continuation of the five years of the currently enrolled patients.

MS. BROGDON: Right. We understand that.

DR. BLANCO: Okay. The panel would also like a better concept of failure of insertion rates once this procedure gets out in the general population, not as a study necessarily but just so that appropriate consent and appropriate information may be given to the patient. You know, I don't know what is a good failure rate for this procedure, but if it is done locally and if it's straightforward and with low risk, I mean, you may be happy to say okay, I'll go do this and fails 20 percent of the time, 30 percent, maybe it will only fail 5, but I'm willing to do it because I've just got to go to the doctor's office and then that's it. I get it done, and if I don't, I get it done another time.

So I think what Dr. Noller was asking was a better understanding of once it gets out in non-expert hysteroscopist hands, what will be the failure of insertion rate? Am I saying that correctly?

DR. ROY: Absolutely. Thank you.

DR. BLANCO: Okay. Does that clarify it for you? It still doesn't look like it does it for you. Okay.

MS. BROGDON: Let me just ask our postmarket

surveillance people. We'll work with what you've already given us. Thank you.

DR. BLANCO: You always do a wonderful job with that.

DR. LARNTZ: Could I comment?

DR. BLANCO: Please.

DR. LARNTZ: I mean, we're asking a question that requires -- I mean, if you do the study right, it could be quite burdensome, and I would argue that it might be easy to do a small observational study with a few physicians to get a notion of this and maybe that's all that would be satisfactory. I don't think we want to mandate getting precise information on this. I think that's actually very difficult to do, very difficult to do right. It would require another study to get this information and to the extent that it probably could be contained in labeling, it probably would take another study to do, and I think that would be -- I'm the statistician. I should be arguing for more data, but in fact, I think if you don't collect the data well, it's not worth too much.

DR. BLANCO: Right.

DR. LARNTZ: And so we've got to be very careful of if we ask for this, I think we're asking for it informally, I think the company understands that, and I think that may be okay, but it's difficult to have any

enforcement on that.

DR. BLANCO: It may be that it may be a better way to approach it as you said, to take some sample of new users and try to get an idea, I think, but I think there is some feeling and maybe, you know, there is some feeling on the panel that we would like some feedback and possible changes in labeling eventually in terms of failure rates once it gets out in more widespread use and without putting much of an onus necessarily on the company to redo, you know, another study.

MS. BROGDON: We can ask the sponsor to make a proposal to the agency later.

DR. O'SULLIVAN: Jorge, I think this becomes important for a lot of reasons. There are always new devices that get out on the market for one reason or another, and in the world of technology, this is increasing more and more, and the point is that all of these things have associated with them costs and who's paying the cost while the patient is the one who is not getting what needs to be gotten or the information is not coming across that this device is not as successful across the board of insertion as it has been, for example?

I mean, there are all kinds of reasons why this can happen, and I think it's very, very important in today's world of technology and as things get released to

be much more rigid. I'm not saying rigid rigid but at least get information for the first four or five years that you've got these devices out there and you're working with them so that you know that they're okay and not wait 25 years to say hello, we've got to bring this back in.

DR. BLANCO: Okay. I think I'm going to go ahead. Go ahead, Ms. Domecus. I'm going to go ahead and take the chairman's prerogative and let you speak.

MS. DOMECUS: Thank you.

I just wanted to clarify that the company already has a plan to gather placement rate and adverse event data on all preceptored cases. So we already have this plan in place.

DR. BLANCO: Thank you.

DR. ROY: But how widespread will your preceptored cases be? I mean, what numbers are we talking about? All?

MS. DOMECUS: That's what we've said. I mean, I imagine at some point, if after a certain period of time, it was a well-established consistent placement rate, we'd go back to the FDA and ask to not do it anymore, but right now, the plan is on all preceptored cases. We have a great interest, too, in making sure that the placement rates are high. We have no interest in anything else.

DR. O'SULLIVAN: I think that fulfills the

need.

DR. LARNTZ: That certainly is adequate and then some, but be very careful to make sure that you're very consistent in collecting those data. It's not easy to get all. It might be better to take a sample and get good information on a sample, but I appreciate what you're saying.

DR. BLANCO: Have we given enough guidance?

MS. BROGDON: Yes.

DR. BLANCO: Great. All right. Any other items? Anything else that we would like to add?

All right. Let me just refresh everybody's memory of what we're going to vote on and then we can have a vote. Basically, as I've written it down and please correct me if I'm wrong, we have a motion on the floor to vote for approval with conditions. The conditions that were included was the hysterosalpingogram at this point be required as was performed in the original study but the committee recommends that the FDA be amenable to having the company bring forth further data on alternative methodologies to look at correct placement and patency to approach changing this particular recommendation.

Number 2. Training, to include knowledgeable hysteroscopists as a prerequisite for beginning to do these. In labeling, we include that we need to clarify the

failure rate and place that and the word that was used was "prominently," that some labeling needs to address -- and I'm going to paraphrase these -- the issue of the young age and potential sequelae, that an issue be noted in the labeling, and these are all labeling issues, about metal sensitivity, electrocautery, and pregnancy subsequent to this procedure, that we have an issue or inclusion about a recommended length for the procedure to the physician and a limit of 1,500 milliliters of saline for use in the patient, again the success rate, that 99.8 percent should be clarified or at least maybe not clarified but something to the effect of the numbers or something that patients can understand with the number of patients that this has been performed in.

A recommendation that the procedure be performed at the proliferative phase of the cycle, that an educational written informed consent be obtained, and the company make an example to be provided to the physicians utilizing this device.

Some recommendations included in the patient pamphlet concerning what to do if you miss a period, a "fallback" plan which just -- what are you going to do if you are one of those where they're unable to insert this in both tubal ostia, definitely recommend the training as previously stated, and then that the continuation of the

observation of the current patients for a total of five years and then a better assessment as has been discussed of the failure of insertion rates for patient counseling and patient labeling.

Did I state those to the satisfaction of the committee? Okay. If there is no other discussion, then let's go ahead and begin with a vote, and you're voting for approval with the prestated conditions. Let's go ahead and start with Dr. Noller.

DR. NOLLER: I vote aye.

DR. DUBEY: I vote aye.

DR. SEIFER: Aye.

DR. BROWN: Yes.

DR. SHARTS-HOPKO: Yes.

DR. O'SULLIVAN: I'm abstaining.

DR. ROY: Yes.

DR. LARNTZ: Yes.

DR. SHIRK: Yes.

DR. BLANCO: The motion passes with a vote of eight yes, zero nos, and one abstention.

As is the custom, we'd like to go around the table and just have a brief mention of why you voted the way you did. Let's begin on this side. Dr. Shirk?

DR. SHIRK: Well, I think this device is as safe as any other devices on the market. Certainly

transcervical sterilization is ideal. I think it may represent a significant improvement in women's health care and so I felt that we should approve the device. I commend Conceptus on their PMA.

DR. BLANCO: Thank you.

DR. LARNTZ: I voted yes because the device clearly met and the studies presented, data presented, clearly met the criteria of safety and effectiveness that are required for approval.

DR. BLANCO: Thank you.

DR. ROY: This device clearly meets those requirements for safety and effectiveness, but I am cognizant of the issues that we've discussed, particularly the use in younger individuals who may not fully appreciate the permanence of the procedure, and I think we've belabored that point sufficiently, that that should be conveyed to anyone who might use it at that age.

DR. BLANCO: Thank you.

DR. O'SULLIVAN: I abstained for religious reasons.

DR. BLANCO: Thank you.

DR. SHARTS-HOPKO: I voted yes because I believe this offers women a less risky, more accessible procedure for permanent sterilization, and I think Conceptus was very thorough in the materials, the large

quantity of materials which you provided.

DR. BLANCO: Thank you.

DR. BROWN: I voted yes because I think the device clearly met the criteria for safety and effectiveness as well as the favorable risk-benefit ratio, particularly since it offers the option of sterilization without general anesthesia which is not basically currently available.

DR. BLANCO: Thank you.

DR. SEIFER: I voted yes because I thought many of the concerns that were voiced during the discussion were addressed in the final vote.

DR. BLANCO: Thank you.

DR. DUBEY: I voted yes the results are very clear. I'm very impressed with the sponsor's data and all the discussion we had in panel to address all borderline issues, and I voted yes for that reasons.

DR. BLANCO: Thank you.

DR. NOLLER: I voted to approve the motion because I feel the company showed that the method is clearly safe and effective and that it has a great chance of improving health care for women in the United States.

DR. BLANCO: Thank you.

I always allow the non-voting members, if they'd like to make a comment at this point, of what they

think, be happy to listen.

MS. LUCKNER: I think this is a great addition to female contraception, and I commend the company. I think our deliberations are not just for today but for tomorrow, and I hope the company proceeds posthaste putting them in place.

DR. BLANCO: And no comment.

I always reserve the right for the last set of comments. I'd like to compliment the company on what I think is one of the best presentations of a PMA that I've seen in eight years here and their data. Thank you very much. It made for a very enjoyable day instead of a very difficult day as we've had a few here in other times.

I also would like to commend the audience for their participation and welcome their comments. Some of them were very good and actually things that we had not thought of and were very good suggestions. We appreciate that, and as always, I'd like to commend everyone at FDA for all of their hard work and wonderful presentations and wonderful participation, and I think you guys do a great job.

So thank you.

With that, unless anyone else would like to make some -- well, if you'd like to make some comments, otherwise we're going to close it up because we're 25

minutes late, and I don't like to be late.

MS. BROGDON: I would just like to thank the panel for your deliberations.

Thank you.

DR. BLANCO: So I'd like to thank the panel, too. It was a great deliberation. Please leave all your paperwork here and they'll get it taken care of with the confidential issues.

Thank you very much. Thank you for your attention. Good night.

(Whereupon, at 5:25 p.m., the meeting was recessed, to reconvene in closed session at 8:00 a.m. on Tuesday, July 23, 2002.)